UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/522,230	01/24/2005	Taeun Park	1751-367	7022

6449 7590 03/28/2007

ROTHWELL, FIGG, ERNST & MANBECK, P.C.
1425 K STREET, N.W.
SUITE 800
WASHINGTON, DC 20005

EXAMINER	
VU, JAKE MINH	
ART UNIT	**PAPER NUMBER**
1618	

SHORTENED STATUTORY PERIOD OF RESPONSE	NOTIFICATION DATE	DELIVERY MODE
3 MONTHS	03/28/2007	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Notice of this Office communication was sent electronically on the above-indicated "Notification Date" and has a shortened statutory period for reply of 3 MONTHS from 03/28/2007.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

PTO-PAT-Email@rfem.com

Office Action Summary	Application No.	Applicant(s)	
	10/522,230	PARK ET AL.	
	Examiner	Art Unit	
	Jake M. Vu	1618	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *05 January 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-16* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-16* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Receipt is acknowledged of Applicant's Arguments/Remarks and Request for Continued Examination filed on 01/05/2007. Claims 1-16 are pending in the instant application.

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 01/05/2007 has been entered.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

Claims 1, 3, 4 and 16 are rejected under 35 U.S.C. 102(a) as being anticipated by TAKETOSHI et al (JP 2001-278810-A; English translated).

Applicant's claims are directed to a composition hybrid of a drug with a layered silicate, such as montmorillonite, and a poorly water-soluble drug, such as itraconazole,

cyclosporine, or carvedilol. Wherein the interlayer cations of the layered silicates are substituted with hydrogen ions to form ionic bonds between the layered silicates and the drug.

TAKETOSHI disclosed a composition hybrid of a drug with a layered silicate (see pg. 13, [0004], such as montmorillonite (see pg. 13, [0004]), and a poorly water-soluble drug (see pg. 13, [0004]), such as cyclosporine (see pg. 10, line 5). Wherein the layered silicates are mixed with water (see pg. 8, line 17; pg. 16, line 1); thus, hydrogen ions from the water would form ionic bonds between the layered silicates and the drug. TAKETOSHI further disclosed the composition is amorphous (see pg. 16, line 10); and the solubility of the poorly water-soluble drug is increased by adding the layered silicate to the drug (see pg. 13, [0004]).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-16 are rejected under 35 U.S.C. 103(a) as being unpatentable over TAKETOSHI et al (cited supra) in view of JUNG et al (*Enhanced solubility and dissolution rate of itraconazole by a solid dispersion technique*. Int J Pharm. 1999 Oct 5;187(2):209-18).

Applicant's claims are directed toward a method for making a hybrid composition comprising of: a layered silicate and a poorly water drug, such as itraconazole, by mixing a layered silicate in an aqueous solution, dissolving a drug in organic solvent; then mixing the solution of layered silicate and dissolved drug together.

As discussed above, TAKETOSHI disclosed a composition hybrid of a drug with a layered silicate (see pg. 13, [0004], such as montmorillonite (see pg. 13, [0004]), and a poorly water-soluble drug (see pg. 13, [0004]), such as cyclosporine (see pg. 10, line 5). Wherein the layered silicates are mixed with water (see pg. 8, line 17; pg. 16, line 1); thus, hydrogen ions from the water would form ionic bonds between the layered silicates and the drug. TAKETOSHI further disclosed the composition is amorphous (see pg. 16, line 10); and the solubility of the poorly water-soluble drug is increased by adding the layered silicate (see pg. 13, [0004]).

TAKETOSI teaches a method for increasing the solubility of a poorly water-soluble drug by mixing an aqueous solution, such as water, an organic solution, the layered silicate, and cyclosporine (see pg. 16 and pg. 10, line 5). Additional disclosures include: to dissolve the layered silicate in water with a pH of 5-6 or less (see 14, [0005]).

TAKETOSHI does not specifically teach using itraconazole as the poorly water-soluble drug, hydroxypropyl methylcellulose or Eudragit E100® in the composition.

JUNG teaches a method of increasing the solubility of a poorly water-soluble drug, such as itraconazole, by incorporating Eudragit E 100 or hydroxypropyl methylcellulose (see Abstract, Introduction and pg. 212).

It would have been obvious to the person of ordinary skill in the art at the time the invention was made to incorporate itraconazole as the poorly water-soluble drug, hydroxypropyl methylcellulose and Eudragit E100® into the TAKEOSHI's composition. The person of ordinary skill in the art would have been motivated to make those modifications, because it would have improved the water-solubility of itraconazole, and reasonably would have expected success because TAKETOSI disclosed cellulose polymers can be added to the composition and any poorly water-soluble drug can be used.

The references do not specifically teach adding the ingredients in the amounts claimed by Applicant. The amount of a specific ingredient in a composition is clearly a result effective parameter that a person of ordinary skill in the art would routinely optimize. Optimization of parameters is a routine practice that would be obvious for a person of ordinary skill in the art to employ and reasonably would expect success. It would have been customary for an artisan of ordinary skill to determine the optimal amount of each ingredient to add in order to best achieve the desired results. Thus, absent some demonstration of unexpected results from the claimed parameters, this optimization of ingredient amount would have been obvious at the time of Applicant's invention.

Response to Arguments

Applicant argues that in the claimed method, a layered silicate and a drug are separately dispersed or dissolved in an aqueous solution and in an organic solvent,

respectively, and then the aqueous solution containing the layered silicate and the organic solvent containing drug are mixed. In contrast, according to paragraph [0007] of Taketoshi, both a drug and a layered silicate are mixed together in an aqueous solution containing aqueous organic solvent, without steps for dispersing or dissolving layered silicates and a drug in a suitable solvent separately. Without these pre-steps, interlayer cations of the layered silicates cannot be substituted with hydrogen ions, which are required for ionic bonds to be formed between the drug and the layered silicates. The Examiner finds this argument unpersuasive, because these pre-steps of dissolving the layered silicates and drug are done simultaneously in TAKETOSHI, wherein the hydrogen ions are from the water dissolving the layered silicate. TAKETOSHI disclosed the same results as Applicant, such as increased solubility of the poorly water-soluble drug and the drug becomes amorphous. Thus, the Examiner finds no criticality of pre-mixing the ingredients individually, when the ingredients will later be mixed together.

Applicant argues that TAKETOSHI cannot have an ionic bond between the drugs and the layered silicates. The Examiner finds this argument unpersuasive, because TAKETOSHI uses the same water as Applicant and water has hydrogen ions; thus, hydrogen ionic bonds do occur. Additionally, TAKETOSHI disclosed calcium ions, potassium ions, etc. could be used (see pg. 15); thus an ionic bond does occur.

Applicant alleges that TAKETOSHI bonds are dipolar bonds and not ionic bonds as claimed by Applicant. The Examiner finds this argument unpersuasive, because TAKETOSHI does not disclose the bonds are dipolar. Additionally, TAKETOSHI used the same ingredients as claimed by Applicant, such as water, organic solvent, layered

silicate, and a poorly water-soluble drug. Thus, the TAKETOSHI's bond must be the same as Applicant.

Applicant argues that TAKETOSHI teaches away from the claimed invention, because TAKETOSHI teaches using acid clay can be treated with alkali to be used as layered silicates for the blended composition. The Examiner finds this argument unpersuasive, because TAKETOSHI teaches this method can also be done with alkali such as calcium, magnesium and aluminum (see [0005], first sentence), which is similar to Applicant's disclosure in the specification of using alkali (see pg. 6, line 17-25).

Telephonic Inquiries

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jake M. Vu whose telephone number is (571) 272-8148. The examiner can normally be reached on Mon-Fri 8:30AM-5:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Hartley can be reached on (571) 272-0616. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Jake M. Vu, PharmD, JD
Art Unit 1618

MICHAEL G. HARTLEY
SUPERVISORY PATENT EXAMINER